Chapter 9

Centers for Genomics and Public Health: An Update

Introduction

During 2001, the Centers for Disease Control and Prevention (CDC), in collaboration with the Association of Schools of Public Health (ASPH), established the first Centers for Genomics and Public Health. These Centers—located at the University of Michigan, the University of North Carolina, and the University of Washington—each quickly became a hub of expertise that built on and complemented existing university programs as well as created new links with local and state health departments. Today, the Centers are recognized national resources for public health genomics that contribute to the knowledge base, provide technical assistance to local, state, and regional public health organizations, and develop and deliver training to the public health workforce.

In initiating this collaborative approach with ASPH, CDC hoped to identify gaps in public health research and to demonstrate, through the use of real examples, the translation of gene discoveries into disease prevention and improved health. This chapter presents an overview of the progress made by the Centers in reaching their goals and objectives over the past four years.

University of Michigan Center for Genomics and Public Health

(*www.sph.umich.edu/genomics/*)

Michigan Center Mission Statement

The Michigan Center for Genomics and Public Health (MCGPH) seeks to integrate genomic discoveries into public health practice, with consideration of the ethical, legal, and social issues associated with the application of these discoveries as well as the involvement of the community at large.

MCGPH projects have included:

- Online Genomics Training: Six Weeks to Genomic Awareness.
- Distance Learning Course: Issues in Public Health Genetics.
- Literature Review: Genetics of Long QT Syndrome.

Online Genomics Training: Six Weeks to Genomic Awareness
Six Weeks to Genomic Awareness is an in-depth, online training series on public health genomics that developed from the collaborative relationship between the MCGPH and the Michigan Department of Community Health (MDCH). The series was designed to provide an understanding of the role of genomics in public health and to reflect the themes most relevant to public health workers, including basic information about molecular genetics, gene-environment interactions, gene-disease associations, genes in populations, genetic testing, genetic resources, and ethical, legal and social (ELSI) implications.

Distance Learning Course: Issues in Public Health Genetics
Issues in Public Health Genetics is a mentored, distance learning, for-credit course that, beginning in January 2005, has been offered to students and public health professionals as a free pilot class and is accessed through Internet broadcasts and CD-ROMs. The course focuses on ethical, legal, and social issues arising from the increasing use of genetic technologies in medicine and public health. In the future, this class will be offered for a fee as part of the regular university curriculum.

Literature Review: Genetics of Long QT Syndrome
Cardiac arrhythmia that causes sudden death is most commonly the result of coronary heart disease. Genetic causes of arrhythmia, however, such as long QT syndrome (LQTS), which affects cardiac ion channels, are increasingly being recognized as having public health consequences. In the United States alone, LQTS is responsible for an estimated 3,000 deaths per year (1). Some arrhythmia susceptibility-conferring genetic polymorphisms have frequencies of 25% or higher in subpopulations in the United States and abroad (2,3).

Channelopathy
Alterations that disturb the formation and function of channels at the cell surface that convey potassium, sodium, calcium, and other ions. Cardiac ion channelopathies can lead to potentially fatal arrhythmias (heart attacks).

Phenotype
The observable properties conferred by one's genetic makeup (contrast with genotype, which is the specific genetic constitution of an individual).

Faculty members at the MCGPH and University of Michigan School of Medicine have reviewed the literature on the long QT syndrome family of cardiac **channelopathies** for the time period 1975-2004. A report entitled The Long QT Syndrome Family of Cardiac Ion Channelopathies (by Stephen M. Modell, MD, MS, and Michael H. Lehmann, MD) has been submitted for publication. This report summarizes published case reports and population-based studies from 20+ countries, as well as research emerging from the International LQTS Registry. Review of the most prevalent and illustrative LQTS mutations and polymorphisms described in this report shows that particular coding regions are structurally more prone to mutations than others and that **phenotypic** severity can depend on mutation site. Gene-gene interactions, in cases where a disease conferring mutation coexists with an LQTS polymorphism, can influence phenotype. Some 10%-15% of LQTS genetic variants are susceptible to triggering by drugs and metabolic disturbances (4). Race-ethnicity and gender can show differential mutation and disease associations, but LQTS is not limited to any one group of people. The report includes family-based and population-screening methodologies

that optimize sensitivity and cost-effectiveness. Breaking developments, such as the commercialization of genetic testing for long QT syndrome, are also covered.

University of North Carolina Center for Genomics and Public Health

(*http://www.sph.unc.edu/nccgph/*)

North Carolina Center Mission Statement

The mission of the North Carolina Center for Genomics and Public Health (NCCGPH) is to foster understanding of the role of genomic information in public health programs and policies for the improvement of human health. This Center focuses on adult onset chronic disease, with an emphasis on cancer.

NCCGPH projects include:

- Breast Cancer Family History Training Module.
- Comprehensive Cancer Control Plan Review for Genomics Components.
- Evaluation of Quality in Promotional Material for Genetic Tests.

Genomic Awareness Campaign

The NCCGPH conducted a needs assessment to evaluate attitudes of public health workers in North Carolina regarding genomics issues. Key informant interviews and focus groups demonstrated that the level of awareness regarding genomics was low and that there was a strong interest in further training in this area. In direct response to the needs assessment, and in response to a request from the North Carolina Division of Public Health, NCCGPH developed a Genomic Awareness Campaign (GAC). The GAC consisted of online training materials and in-person presentations that were made available to personnel in local health departments. The training materials include basic definitions of genomics and genetics, the relationship between genomics and public health, case studies, and questions for discussion. NCCGPH created the GAC with the involvement and advice of senior staff in the NC Division of Public Health to best tailor the content and presentation style to personnel in local health departments.

NCCGPH has conducted the GAC presentation at two annual meetings of the North Carolina Association of Public Health Nurse Administrators and at the annual meeting of the NC Dietetics Association, which is attended by registered dieticians in public health and private practice. It has also been presented to local public health departments throughout the state. GAC training and other materials can be viewed at the NCCGPH website under "Tools" (*www.sph.unc.edu/nccgph/tools/index.htm*).

Breast Cancer Family History Training Module
One familiar genomic tool that is currently accepted and applied in nursing practice is the collection of a family history. Although public health nurses are trained to obtain a family history from each of their patients, the information is not comprehensive enough to identify potential genetic conditions (5). The NCCGPH developed a Breast Cancer Family History Training Module for public health nurses through a formative evaluation process. This training module includes basic definitions of inheritance patterns; how to draw and interpret a pedigree; and how to classify women as low, medium and high-risk for breast cancer based on their family history and personal risk factor profile. Several case studies are included. The module incorporates "lessons learned" from nurses in public health practice; these lessons include recommendations that educational material should build upon existing knowledge, feature case studies, and be presented in a form that is comprehensible to persons with varying scientific backgrounds. The module combines established training principles from both the nursing and health education literature. The module is available for distribution, although it is not available online. For more information, contact NCCGPH.

Comprehensive Cancer Control Plan Review for Genomics Components
The CDC identified state Comprehensive Cancer Control (CCC) plans that mentioned genomics or genetics, and NCCGPH reviewed these **cancer control plans** in detail. The assessment included a review of CCC plan content as well as successes and barriers for implementation of genomics-related cancer control initiatives. The project was conducted in two phases: a content analysis of 30 written state CCC plans for genomics components, followed by telephone interviews with CCC plan coordinators in the 16 states that had CCC plans with genomics components.

Cancer control plans
Comprehensive documents produced by state health departments to address screening, treatment and prevention of cancer.

Most states emphasized raising awareness and educating health care providers and the public about the role of genomics in cancer control. Many states considered awareness of family history to be an important aspect of their CCC plans. Approximately two-thirds of states with family history components in their plans had already begun to implement them. Adequate funding and productive partnerships improved the likelihood of implementation success. Virtually all of the state CCC coordinators reported that they would benefit from additional training in cancer genetics and public health genomics such as cancer control plans (6).

Evaluation of Quality in Promotional Material for Genetic Tests
Many commercial genetic tests are now available to the public. Some of these tests are designed to identify genes or gene products that are present with increased frequency in people with certain types of illness, disease, or other health conditions. Other genetic tests and products have more social or legal

applications, such as ancestry profiling, biological relationship testing, and DNA banking. The NCCGPH is currently conducting a comprehensive and systematic evaluation of promotional material for genetic tests and products that are accessible to consumers on the World Wide Web. Topics of interest include persuasive tactics used in promotional materials, quality and accuracy of information presented, and characteristics of target audiences. The project will be completed during 2006, after which the results will be published. A PowerPoint presentation of this project is available at *www.sph.unc.edu/nccgph*. *For more information on this topic, see Chapter 4, Direct-to-Consumer Marketing Campaign: Evaluation of Quality in Promotional Material for Genetic Tests for Susceptibility to Breast and Ovarian Cancer.*

University of Washington Center for Genomics and Public Health

(*http://depts.washington.edu/cgph/*)

University of Washington Center Mission Statement

The University of Washington Center for Genomics and Public Health (UWCGPH) seeks to integrate advances in genetic technology into public health practice and offer research and educational opportunities for public health students and professionals.

UWCGPH projects include:

- Knowledge Base Development: Human Genome Epidemiology (HuGE) Reviews.
- Training: Teleconference on the Genomics of Obesity.
- Technical Assistance:
  1. Genomics Survey Coordination Workgroup
  2. Interactive Brown Bag on Public Health Genomics.

Knowledge Base Development: Human Genome Epidemiology (HuGE) Reviews

Faculty and students at the UWCGPH performed an in-depth review of the genetic and epidemiological literature on familial hypercholesterolemia (FH). The genetics of this disease have been extensively studied since the 1930s. Characteristics of FH include elevated cholesterol levels, **xanthomata**, and a family history of premature heart disease. The clinical FH phenotype results from mutations in the low-density lipoprotein receptor gene (*LDLR*) and the apolipoprotein-B 100 gene (*APOB*). Because of the breadth of the subject material, the review was separated into three papers, all of which were published in the American Journal of Epidemiology and are available on the HuGE website (7-9).

Xanthomata
Localized collections of cells containing lipid material, including cholesterol and triglycerides.

- The Prevalence Review describes current diagnostic tools for FH, catalogues prevalence studies of *LDLR* and *APOB* mutations in FH subjects, and assesses FH screening programs (7).

- The Association Review evaluates association studies of clinical FH, as well as specific mutations in *LDLR* and *APOB*, with coronary heart disease (8).

- The Mini-Review summarizes studies of FH as a potential risk factor for peripheral vascular and ischemic cerebrovascular disease (9).

These reviews identified several areas for future research, including:

- Examining the role of gene-environment interactions in FH.

- Assessing the strength of the association between incident **ischemic stroke** events and FH.

- Evaluating the public health impact of genetic FH screening programs.

Ischemic stroke
Ischemic stroke is caused by blockage in an artery that supplies blood to the brain, resulting in a deficiency in blood flow (ischemia).

Training: Teleconference on the Genomics of Obesity
In collaboration with the Chronic Disease Program directors and the CDC Division of Nutrition and Physical Activity, the director of the UWCGPH, Karen L. Edwards, PhD, presented an October 2004 teleconference on Obesity: Current Topics in Genetics. Objectives for participants were to:

- Be familiar with the evidence for genetic influences on obesity.

- Understand how genetic factors can influence obesity, both directly and indirectly.

- Be familiar with one current application of genomic information for public health practice.

Materials from the teleconference, including an audio-assisted slide presentation and an informational brochure, are available on the UWCGPH website (*http://depts.washington.edu/cgph/centergoals/obesity.htm*).

Technical Assistance
Technical assistance was provided at two events, the Genomics Survey Coordination Workgroup and the Interactive Brown Bag on Public Health Genomics.

Genomics Survey Coordination Workgroup
The UWCGPH established a workgroup of representatives from state health departments interested in collecting data on various genomics-related topics, including family history, through population-based surveys, such as the Behavioral Risk Factor Surveillance System (BRFSS).

The workgroup was comprised of epidemiologists and genomics program coordinators from state health agencies in Michigan, Minnesota, North Carolina, Oregon, and Utah as well as representatives from the CDC Office of Genomics and Disease Prevention (OGDP) and the Centers for Genomics and Public Health. One focus of the workgroup was to evaluate the potential of this population-based data for a variety of public health activities, including:

- Assessing the prevalence of a positive family history of disease.
- Monitoring trends in prevalence of family history of disease.
- Gauging public awareness of family history as a risk factor for disease.
- Tracking provider practices regarding the collection of family history information.
- Understanding how family history contributes to patients' perceptions of risk.
- Investigating beliefs about the ability to modify risk by changing lifestyle factors.

Interactive Brown Bag on Public Health Genomics
In collaboration with the Oregon Department of Human Services (ODHS) Genetics Program, the UWCGPH developed materials for an interactive brown bag session designed to generate interest in genomics for public health audiences. The materials used at the session—including PowerPoint slides, a discussion guide, supplemental reading materials, and an evaluation plan—covered the following six topics:

- Genetic testing for inherited cancer disposition.
- Lifestyle advice.
- Newborn screening.
- Cancer treatment and genetics.

- Workplace testing.
- Reproductive genetics.

These materials have been organized into a package and are available for distribution, although they are not available online. For more information, contact UWCGPH.

Centers' Collaborative Activities with CDC

The three Centers for Genomics and Public Health also worked in collaboration with OGDP to develop an online presentation called Genomics for Public Health Practitioners. This 45-minute presentation is intended for public health practitioners who have minimal experience in genomics and would like to learn more about the relevance of genomics to public health. The program can be accessed at: *www.cdc.gov/genomics/training/GPHP/default.htm*.

The Centers also contributed to a genomics issue of the online Preventing Chronic Disease Journal. Articles can be accessed at: *www.cdc.gov/pcd/issues/2005/apr/toc.htm*.

Summary of the Centers' Activities

The Centers for Genomics and Public Health have become recognized national resources in public health genomics and have increased the capacity of the public health workforce to use genomics information to improve the health of populations. These Centers have established the infrastructure, understanding, and credibility to translate genomics information and discoveries into public health practice and are considered leaders in translating and applying genomic concepts and applications to public health practice.

References

1. Vincent GM. Long QT syndrome. Cardiology Clinics 2000;18:309-25.
2. Ackerman MJ, Tester DJ, Jones GS, Will ML, Burrow CR, Curran ME. Ethnic differences in cardiac potassium channel variants: implications for genetic susceptibility to sudden cardiac death and genetic testing for congenital long QT syndrome. Mayo Clin Proc 2003;78:1479-87.
3. Laitinen P, Fodstad H, Piipo K, Swan H, Toivonen L, Viitasalo M, et al. Survey of the coding region of the HERG gene in long QT syndrome reveals six novel mutations and an amino acid polymorphism with possible phenotypic effects. Human Mutation 2000;15:1-6.
4. Yang P, Kanki H, Drolet B, Yang T, Wei J, Viswanathan PC, et al. Allelic variants in long-QT disease genes in patients with drug-associated torsades de pointes. Circulation 2002;105:1943-8.

5. Irwin D, Millikan R, Stevens R, Roche M, Rakhra-Burris T, Davis M, et al; Genomics and Public Health Practice: A Survey of Nurses in Local Health Departments in North Carolina. Journal of Public Health Management and Practice 2004;10(6):539-44.

6. Irwin DE, Zuiker ES, Rakhra-Burris T, Millikan RC. Review of state Comprehensive Cancer Control plans for genomics content. Preventing Chronic Disease [serial online] 2005 Apr [cited 2005 Apr 27]. Available from URL: *http://www.cdc.gov/pcd/issues/2005/apr/04_0128.htm*.

7. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. American Journal of Epidemiology [online] 2004 [cited 2005 Aug 15] 160(5):407-20. Available from URL: *http://www.cdc.gov/genomics/hugenet/reviews_arch.htm#Cardio*.

8. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Familial hypercholesterolemia and coronary heart disease: a HuGE association review. American Journal of Epidemiology [online] 2004 [cited 2005 Aug 15] 160(5):421-9. Available from URL: *http://www.cdc.gov/genomics/hugenet/reviews_arch.htm#Cardio*.

9. Hutter CM, Austin MA, Humphries SE, Zimmern RL. Familial hypercholesterolemia, peripheral arterial disease, and stroke: a HuGE mini review. American Journal of Epidemiology [online] 2004 [cited 2005 Aug 15]160(5):430-5. Available from URL: *http://www.cdc.gov/genomics/hugenet/reviews_arch.htm#Cardio*.

Michigan

Contact Information

Michigan Center for Genomics and Public Health (MCGPH)
University of Michigan
School of Public Health
611 Church Street, Room 258
Ann Arbor, MI 48104-3028
Phone: (734) 615-3412
Fax: (734) 998-6798
Email: *mcgph@umich.edu*

Authors

Jennifer Bodzin, Stephen M. Modell, Jessica Nelson, Michael H. Lehmann, Sharon L. R. Kardia, and Toby Citrin

North Carolina

Contact Information

North Carolina Center for Genomics and Public Health (NCCGPH)
The North Carolina Institute for Public Health
Campus Box 8165
The University of North Carolina at Chapel Hill
Chapel Hill, NC 27599
Phone: (919) 966-9834
Fax: (919) 966-0478
Email: *phgenomics@unc.edu*

Authors

Robert C. Millikan, Debra E. Irwin, Mary V. Davis, Myra Roche, Elizabeth Mahanna, and Tejinder K. Rakhra-Burris

Special thanks to Heather Keith, Evaluation Graduate Assistant, Masters Candidate, and Rene Sterling, MHA, Graduate Research Assistant, Doctoral Candidate, University of North Carolina School of Public Health.

Washington

Contact Information

University of Washington Center for Genomics and Public Health (UWCGPH)
The University of Washington
Box 354695
4225 Roosevelt Way, NE
Seattle, WA 98105
Phone: (206) 616-6917
Fax: (206) 616-0688
Email: *cgph@u.washington.edu*

Authors

Karen Edwards, Tabitha Harrison, and Sarah Raup